PRE-SCREENING COMPOUND AUTHORIZATION AND CONSENT TO DONATE TUMOR TISSUE FOR HER2 TESTING

YALE UNIVERSITY SCHOOL OF MEDICINE – YALE-NEW HAVEN HOSPITAL: SMILOW CANCER HOSPITAL

200 FR. 4 (2014-11)

Study Title: HER2CLIMB (ONT-380-206): Phase 2 Randomized, Double-Blinded, Controlled Study of ONT-380 vs. Placebo in Combination with Capecitabine and Trastuzumab in Patients with Pretreated Unresectable Locally Advanced or Metastatic HER2+ Breast Carcinoma

Principal Investigator: Michael DiGiovanna, MD, PhD
Principal Investigator's Phone Number: 203-737-8309
24-Hour Phone Number: 203-785-4191
Principal Investigator's Mailing Address: 300 George Street, Suite 120, New Haven, CT 06511

Funding Source: Cascadian Therapeutics, Inc.

Pre-screening

Invitation to Participate and Description of Project

This consent form is called a "Pre-screening Compound Authorization and Consent form" in which you are invited to provide a research sample and you are being asked to give permission for research tests to be performed on your cancer tissue sample. If you agree to participate, this cancer tissue sample will be tested to see if your breast cancer has high levels of a protein called HER2. You have been asked to take part in this testing because you have been diagnosed with advanced breast cancer and are being considered for participation in the main portion of a clinical study, HER2CLIMB (ONT-380-206). Having your tissue tested now will help determine whether you may be eligible to enroll in the HER2CLIMB study, if you decide to do so in the future. If this pre-screening test shows that your breast cancer tissue qualifies for the HER2CLIMB study, you may be given more information about that study and another consent form that describes the study drug being tested.

In order to decide whether or not you wish to be participate in pre-screening for HER2CLIMB, you should know enough about its risks and benefits to make an informed decision. This consent form gives you detailed information about the pre-screening, which a member of the research team will discuss with you. This discussion should go over all aspects of this research: the purpose of the pre-screening, the procedures that will be performed, the risks, possible benefits, possible alternative options, your rights as a participant and other information about the pre-screening. You should take whatever time you need to discuss this information with your

physician and family. The decision to participate or not is yours. Once you understand the pre-screening, you will be asked if you wish to participate; if so, you will be asked to sign and date where indicated on this form.

The pre-screening is being sponsored by Cascadian Therapeutics, Incorporated (Inc.). Cascadian Therapeutics, Inc. is called the Sponsor and Yale University is being paid by Cascadian Therapeutics, Inc. to conduct this pre-screening. Dr. Michael DiGiovanna is the principal investigator of this pre-screening research and of the main research study (Study HER2CLIMB) at Yale Cancer Center.

Purpose

The purpose of this pre-screening consent form is to tell you about having a sample of your tumor tested. The purpose of this pre-screening testing is to test a sample of your tumor to see if your breast cancer has a protein called HER2. If the results show that your breast cancer does contain the HER2 protein, you may be invited to take part in the main research study (HER2CLIMB). At that time, you will be given more information about the main research study and you will also be given a different consent form that describes the main research study. It is possible that this pre-screening test may show that you cannot take part in the main research study (HER2CLIMB). If this happens, your doctor will discuss this with you.

It is expected that 180 subjects will participate in the main research study at 90 sites in North America and 19 sites in Western Europe. It is expected that approximately 14 subjects will be enrolled in the main research study at Yale Cancer Center.

Procedures

All of the procedures listed below that will be performed are being done for research purposes only and are not considered standard of care. You will only have these procedures done if you agree to participate in this pre-screening.

By signing this pre-screening compound authorization and consent form, you are agreeing to allow a portion of a previous tumor sample to be tested by a research laboratory, or to have a new biopsy (the removal of tissue from your tumor), to test whether your tumor cells contain HER2 protein. This testing is needed to determine if you are eligible to participate in the main research study (HER2CLIMB). You may ask your doctor for the results of this test. If you have questions about what the results of the test may mean for you, or if you would like more information about the tests and procedures that will be done as a part of the tissue testing, you should discuss this with your study doctor.

It may take up to 4 weeks before results are known.

Potential Risks, Side Effects, Discomforts and Inconveniences

Obtaining Archival Tumor Tissue (if your archival tumor tissue is available):
A sample of your original tumor tissue has previously been collected for another purpose and there is enough tumor tissue available for use in this pre-screening. Your study doctor will request that a small sample of your original tumor be sent to a laboratory for testing. There are no additional physical risks involved in this testing.

Tumor Biopsy (if your archival tumor tissue is not available, or not enough of it is available):
As with any procedure, there are risks and discomforts. You may feel some amount of pain or discomfort during a biopsy, including slight, stinging pain when a local anesthetic is injected by needle to numb the area, pressure and dull pain where the biopsy needle is inserted, discomfort from lying still for an extended time, and soreness, inflammation, bleeding, swelling, and/or infection at the biopsy site. With a tumor biopsy, there is a rare possibility of tumor cells spreading into the nearby area. If a general anesthetic is used, you will not feel pain during the procedure because you will be asleep. Your physician will explain the details of the procedure and the risks to you, depending on how the biopsy will be obtained.

For more information about risks and side effects, ask the researcher or contact their office at (203) 737-8309.

Benefits

If you agree to take part in pre-screening, we cannot guarantee that you will receive any benefits.

Economic Considerations

You will not be paid for taking part in this pre-screening. There will be no cost to you or your insurance provider for taking part in this pre-screening. The sponsor will pay for any procedures that are not considered standard care for patients with your disease. These include:

- Tumor biopsy sample

If you have questions regarding this information, you may call Dr. Michael DiGiovanna's office for assistance at 203-737-8309.

Alternatives Options

You do not have to participate in this pre-screening but if you do not, then you cannot be considered for enrollment in the main research study.

Talk to your doctor about your choices before you decide if you will take part in this pre-screening.

Confidentiality and Authorization to collect, use and disclose Protected Health Information

Your consent to participate in the pre-screening means you agree that Yale University, Yale-New Haven Hospital, and Dr. Michael DiGiovanna obtain your medical information that they request for pre-screening purposes from your physicians and your other health care providers from the past or during your participation. The protected health information that will be collected in this pre-screening includes tumor tissue sample, name, sex, date of birth, medical records, and other information. This health information will be used by and/ or disclosed to (shared with) the laboratory chosen by Cascadian Therapeutics, Inc. to perform the testing.

Any identifiable information that is obtained in connection with this pre-screening will remain confidential and will be disclosed only with your permission or as permitted by U.S. or State law. Examples of information that we are legally required to disclose include abuse of a child or elderly person, or certain reportable diseases such as HIV or hepatitis. When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity unless your specific consent for this activity is obtained.

We understand that information about you obtained in connection with your health is personal, and we are committed to protecting the privacy of that information. If you decide to be in this pre-screening, the study staff will get information that identifies you and your protected health information. This may include information that might directly identify you, such as your name, date of birth, and medical record number**.** This information will be de-identified prior to providing it to the sponsor, meaning we will replace your identifying information with a code that does not directly identify you. The study doctor will keep a link that identifies you to your coded information, and this link will be kept secure and available only to the Principal Investigator or selected members of the study team. Any information that can identify you will remain confidential.

The records for this trial will be stored in locked cabinets and/or offices and password protected computers. The study team will only give this coded information to others to carry out this pre-screening research or to sponsor representatives to comply with federal laws and regulations. It is anticipated that records containing the information that links you to your coded information will be maintained indefinitely, as there are no plans at this time to destroy these records at the end of the pre-screening research.

Information about your pre-screening participation will be entered into your Electronic Medical Record (EMR). Once placed in your EMR, these results are accessible to all of your providers who participate in the EMR system. Information within your EMR may also be shared with

others who are appropriate to have access to your EMR (e.g., health insurance company, disability provider.)

Information about you and your health which might identify you may be used by or given to:

- The U.S. Department of Health and Human Services (DHHS) agencies
- Representatives from Yale University and the Human Investigation Committee (the committee or Institutional Review Board that reviews, approves, and monitors testing and research on human subjects), who are responsible for ensuring research compliance. These individuals are required to keep all information confidential
- Your providers who are participants in the Electronic Medical Record (EMR) system
- Those individuals at Yale who are responsible for the financial oversight of research including billings and payments
- The testing and study doctor, Michael DiGiovanna, MD, PhD, and the Yale study team
- The U.S. Food and Drug Administration (FDA). This is done so that the FDA can review information about the new drug product involved in this research. The information may also be used to meet the reporting requirements of drug regulatory agencies.
- Other federal regulatory or governmental agencies such as the National Cancer Institute/National Institutes of Health (NCI/NIH) and the Office for Human Research Protections (OHRP)
- The testing and study sponsor or manufacturer of study drug, Cascadian Therapeutics, Inc., and/ or their representatives, affiliates, and collaborators
- People and companies with whom the sponsor works, such as clinical research organizations who help the sponsor manage the testing and the main research study
- Drug regulatory agencies in other countries
- Governmental agencies to whom certain diseases (reportable diseases) must be reported
- Health care providers who provide services to you in connection with this testing.
- Laboratories and other individuals and organizations that analyze your health information in connection with this testing, according to the testing plan.
- Data and Safety Monitoring Boards and others authorized to monitor the conduct of the testing
- Independent committee of physicians and experts that will review safety information from this testing periodically
- Individuals and businesses outside the hospital that provide services (for example, insurance companies, legal offices, and data storage companies)
- Medical information from this testing may become part of your medical record at the clinic, and, in order to provide you with routine care, other people at the clinic may need to review the information we put into your record.

This consent is for obtaining and testing of a tumor sample. The tissue specimen obtained for the pre-screening purposes will be provided to the sponsor of this testing, Cascadian Therapeutics, Inc., and its authorized representatives and affiliates. This specimen will not include information that identifies you directly. Once you provide the specimen you will not have access to it. The specimen will be used for pre-screening testing purposes, and such use may result in discoveries that could become the basis for new products or therapeutic agents. In some instances, these discoveries may be of potential commercial value. You will not receive any money or other benefits derived from such a product.

The Sponsor and sponsor's authorized representatives will analyze and use the information they receive for the purposes of this testing. Such purposes include:

- Conducting and overseeing the testing
- Checking your suitability to take part in the testing

By signing this form, you authorize the use and/or disclosure of the information described above for this testing. The purpose for the uses and disclosures you are authorizing is to ensure that the information relating to this research is available to all parties who may need it for research purposes.

All health care providers subject to HIPAA (Health Insurance Portability and Accountability Act) are required to protect the privacy of your information. The research staff at Yale School of Medicine and Yale-New Haven Hospital is required to comply with HIPAA and to ensure the confidentiality of your information. Some of the individuals or agencies listed above may not be subject to HIPAA and therefore may not be required to provide the same type of confidentiality protection. They could use or disclose your information in ways not mentioned in this form. However, to better protect your health information, agreements are in place with these individuals and/or companies that require that they keep your information confidential.

Those who receive your information may share it if they are required by law to do so. If you receive Medicare benefits and if the sponsor of this testing pays for any testing-related treatment, then complications or injuries, personal information about you, your treatment, and your participation in this testing will be provided to the sponsor, who will provide it to Medicare to the extent required by law.

You have the right to review and copy your health information in your medical record throughout the pre-screening process in accordance with institutional medical records policies.

This authorization to use and disclose your health information collected during your participation in this pre-screening will never expire.

In Case of Injury

If you are injured as a result of your participation in this pre-screening testing, promptly tell the testing and study doctor in person or call him/her at the number listed at the top of this form.

You will get medical treatment if you are injured as a result of taking part in this testing. Your doctor will explain the treatment options to you and tell you where you can get treatment. The costs of the treatment may be covered by sponsor of the testing, Cascadian Therapeutics, Inc., or billed to you or your insurer just like other medical costs, depending on a number of factors. Cascadian Therapeutics, Inc. does not normally provide any other form of compensation for injury.

You do not give up any of your legal rights to seek payment for testing-related injuries by signing this form or by agreeing to participate in this testing.

Voluntary Participation and Withdrawal

You are free to choose not to take part in pre-screening. Refusing to take part in this pre-screening will not lead to penalty or loss of benefits to which you are otherwise entitled (such as your health care outside the testing, the payment for your health care, and your health care benefits). However, you will not be able to enroll in this pre-screening testing and will not receive pre-screening testing as a participant if you do not allow use of your information as part of this study.

If you decide to participate in this pre-screening, you are free to stop and withdraw from this portion of the study at any time during its course. To withdraw from the pre-screening, you can call a member of the research team at any time and tell them that you no longer want to take part. The sponsor will need to retain and use any research results, and may need to retain and use any samples, that have already been collected. The sponsor must do this to comply with its legal obligations and to maintain the scientific integrity of the testing.

Withdrawing From the Pre-screening:
If you decide to participate in this pre-screening, you are free to stop and withdraw from this pre-screening research at any time during its course. To withdraw from the pre-screening, you can call a member of the research team at any time and tell them that you no longer want to take part.

The researchers may withdraw you from participating in the pre-screening procedures if necessary.

If you choose not to participate or if you withdraw it will not harm your relationship with your with your own doctors or with Yale-New Haven Hospital.

If you fail to give your consent by not signing this document, or if you cancel your consent later, then you will not be eligible to participate in the pre-screening or the main research study (HER2CLIMB), and will not receive any treatment provided as part of the main research study (HER2CLIMB). Unless and until you do cancel the consent, it will remain valid and effective.

Withdrawing Your Authorization to Use and Disclose Your Health Information:
You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the testing and study doctor, Dr. Michael DiGiovanna, at the address listed on page one of this form. If you withdraw your permission, you will not be able to participate in the pre-screening testing or the main research study (HER2CLIMB).

When you withdraw your permission, no new health information identifying you will be gathered after that date. If you go on to sign consent for participation in the main research study (HER2CLIMB), information that has already been gathered may still be used and given to others until the end of the main research study, as necessary to insure the integrity of the study and/or study oversight.

Questions
We have used some technical terms in this form. Please feel free to ask about anything you don't understand and to consider this research and the consent form carefully – as long as you feel is necessary – before you make a decision.

Authorization and Permission

I have read (or someone has read to me) this form and have decided to participate in the project as described above. Its general purposes, the particulars of my involvement and possible hazards and inconveniences have been explained to my satisfaction. My signature also indicates that I have received a signed and dated copy of this consent form.

By signing this form, I give permission to the researchers to use and give out information about me for the purposes described in this form. By refusing to give permission, I understand that I will not be able to participate in this research.

Pre-screening Participant (print name)	Signature	Date
Person obtaining consent (print name)	Signature	Date
Person obtaining consent (print name) – only if applicable, otherwise blank	Signature	Date
Interpreter/ Witness (print name) – only if applicable, otherwise blank	Signature	Date

If after you have signed this form you have any questions about your privacy rights, please contact the Yale Privacy Officer at (203) 432-5919.

If you have further questions about this project or if you have a research-related problem, you may contact the Principal Investigator, Dr. Michael DiGiovanna, at 203-737-8309. If you would like to talk with someone other than the researchers to discuss problems, concerns, and questions you may have concerning this research, or to discuss your rights as a research subject, you may contact the Yale Human Investigation Committee at (203) 785-4688.